$7.8 million) each over 2 years on top of existing annual funding of between £3 million and £4 million (between about $4.7 million and $6.2 million) each. The centers will act as hubs of research in areas of strategic importance to CRUK, and will facilitate collaboration among investigators across CRUK's 15 centers.

"We are substantially increasing funding to develop more comprehensive centers with the expertise, infrastructure, and technology required to deliver translational research at the highest international level," says David Scott, PhD, CRUK's director of Discovery Research and Centers. "We hope to increase the level of investment in these locations over the next few years as research activity ramps up."

At Cambridge, the new funding will support development of early-detection techniques for different cancers, says Scott. Investigators are also building a brain cancer program under the direction of Richard Gilbertson, MD, PhD, who most recently served as director of the Comprehensive Cancer Center at St. Jude Children's Research Hospital in Memphis, TN.

In Manchester, researchers will establish a national center to discover biomarkers for early detection, clinical decision-making, and monitoring treatment, says Scott. The center already has expertise in circulating tumor cells (CTC), and investigators there published findings last year showing that CTCs could be used to monitor small-cell lung cancer and predict response to treatment (Nat Med 2014;20:897–903). In addition, the Manchester center has partnered with the CRUK center at University College London to establish a Center of Excellence in lung cancer.

Researchers at Oxford's Clinical Imaging and Radiation Oncology Hub are exploiting insights from basic biology to improve radiotherapy. For example, they recently published findings suggesting that giving AKT inhibitors in combination with radiotherapy might improve the response to radiotherapy in p53-deficient tumors (J Clin Invest 2015;125:2385–98).

"We think of this new funding as a way to bridge the gap between the lab and the clinic," says Scott. "It's providing the infrastructure, such as data managers, biobanking, and platforms, to profile tumors at the molecular level—the things that enable translational research."

Such discovery is critical given that the 10-year survival rate in the UK for all cancers is about 50%. "We'd like to see that increase to at least 75% over the next 20 years," Scott says. ■

New Compound Targets Warburg Effect

Researchers have developed a drug that kills cancer cells by inhibiting lipid production and the Warburg effect, the tendency for tumors to rely heavily on glycolysis even when a more efficient way of metabolizing glucose is available. The drug induces cell death in multiple cancer types and does not cause the side effects that have derailed previous attempts to target these processes.

"It's hitting two of the major metabolic pathways that cancer cells like to use," says senior author Tom Burris, PhD, chair of the pharmacology and physiology department at the St. Louis University School of Medicine in Missouri.

Researchers do not fully understand how the Warburg effect helps cancer cells, but it may aid cellular proliferation—and thus give tumors a growth advantage—by increasing production of metabolites that can be converted to lipids, amino acids, and nucleotides. Scientists have tried to design drugs to target specific enzymes in glycolysis or lipogenesis. However, most glycolysis inhibitors have been ineffective or killed normal cells, and lipogenesis inhibitors have caused side effects, such as anorexia and weight loss.

The agent developed by Burris's team, SR9243, targets the nuclear receptors LXRα and LXRβ. These receptors activate expression of glycolysis and lipogenesis enzymes. The drug prompts the receptors to bind co-repressor proteins that reduce expression of those enzymes instead.

The drug killed colorectal, lung, and prostate cancer cells in cell culture but did not affect healthy cells, the team reports (Cancer Cell 2015;28:42–56). Expression of glycolysis and lipogenesis genes dropped, as did levels of glycolysis metabolites and lipids. In mice with xenografts of these cancers, the drug slowed tumor growth and did not cause weight loss, liver toxicity, or inflammation of normal tissue.

That the drug worked in different types of cancer cells is encouraging, says Ralph DeBerardinis, MD, PhD, chief of the division of pediatric genetics and metabolism at The University of Texas Southwestern Medical Center in Dallas, who wasn't involved in the study. "It means that if the therapy turned out to be effective, it wouldn't be tied to a small subset of human cancers. It could potentially be fairly general."

Burris's team found some limitations, however. SR9243 was less potent in pancreatic and ovarian cancers and had no effect on breast tumor cell lines, says Burris. He and his colleagues are investigating why these cancers don't respond well to the treatment.

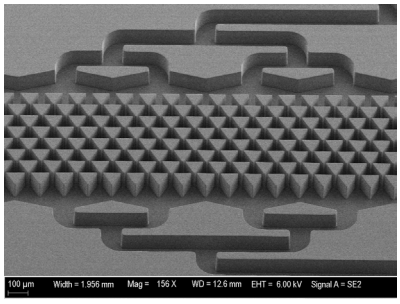
DeBerardinis also cautions that scientists still know little about which metabolic pathways are active in a human tumor. "The metabolism of an actual tumor in a person is a black box," he says. He would like to see the drug tested in mice with tumors that arise spontaneously rather than from an injected cell line, because their metabolism may be more similar to that of a human patient's tumor than tumors established from xenografts. ■

Device Captures CTC Clusters in Blood

Individual blood-borne tumor cells have been linked to metastasis in patients with cancer, and clusters of these circulating tumor cells (CTC) spell an even worse prognosis. To facilitate the study of these aggregates, researchers have created Cluster-Chip, a microfluidic device that captures CTC clusters directly from the blood without using antibodies or chemical labels.

Isolating CTCs is tricky because they are uncommon—about one per billion cells in blood—and CTC clusters are rarer still. Many methods use antibodies, which bind CTCs in order to capture them directly or bind other blood cells in order to separate them from CTCs. However, because antibody strength and specificity often vary and CTCs can be heterogeneous in their expression of surface markers, antibody-based techniques are not ideal.

Cluster-Chip, on the other hand, is "antigen-agnostic," says A. Fatih

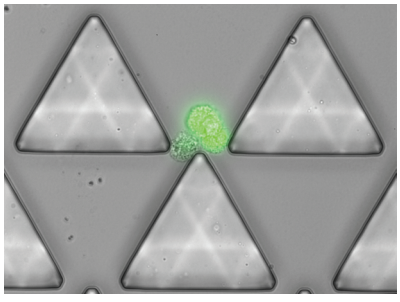


A. Fatih Sarioglu

Scanning electron micrograph of Cluster-Chip shows rows of triangular pillars that trap CTC clusters.

Sarioglu, PhD, a biomedical engineer at Georgia Institute of Technology in Atlanta. Unlike other methods that target single CTCs with the hope of capturing clusters, the new device, Sarioglu says, is specifically designed to catch clumps of CTCs.

Sarioglu and molecular biologist Nicola Aceto, PhD, of Massachusetts General Hospital (MGH) in Boston, are co–first authors of a paper describing Cluster-Chip (Nat Methods 2015;12:685–91). They initiated the research while working with Mehmet Toner, PhD, and Daniel Haber, MD, PhD, at MGH.



A. Fatih Sarioglu

A three-cell cluster of fluorescently labeled human prostate adenocarcinoma cells captured on Cluster-Chip.

Measuring about 7.50 cm × 3.75 cm, Cluster-Chip is a glass slide that traps CTC clusters as blood passes through a matrix of triangular pillars with 12-µm gaps between vertices. Although CTCs are slightly larger (about 15 µm wide), single cells are squishy and easily squeeze through the matrix. However, CTC clusters catch on the points of the triangular pillars and remain trapped on the slide.

To measure the device's capture efficiency, the researchers spiked healthy human blood samples with clusters of fluorescently labeled MDA-MB-231 human breast cancer cells. Cluster-Chip captured 99% of clusters containing at least four tumor cells, 70% of three-cell clusters and 41% of two-cell clusters. For optimal performance, the researchers used a flow rate about 10 times slower than normal blood circulation and processed samples at 4°C instead of room temperature.

Compared with other methods, Sarioglu says, Cluster-Chip may give a truer estimate of how common CTC clusters are. When used on blood samples from 60 patients with metastatic breast or prostate cancer or with melanoma, CTC clusters were found in 30% to 40% of patients. Earlier experiments with antibody-based microfluidic tools developed by the same researchers detected CTC clusters in only 5% to 10% of patient samples.

Chwee Teck Lim, PhD, of the National University of Singapore, says devices like Cluster-Chip provide a "means of capturing circulating tumor microemboli." Isolating CTC clusters can give insight into their role and function, including how they might differ from single CTCs. For example, "Do CTC clusters contain specific subpopulations of CTCs that make them more likely to metastasize?" Lim asks. "We do not know yet." ■

AIM2 Blocks Colon Cancer in Three Ways

Two recent papers explain how the inflammasome protein AIM2 protects against colon cancer, suggesting strategies to prevent and treat the disease.

AIM2 detects double-stranded DNA from bacteria and viruses and forms part of the inflammasome, an infection-fighting protein complex. Previous research also suggests that AIM2 is a tumor suppressor because its expression is turned down or off in many melanomas, colorectal cancers, and prostate tumors. However, researchers don't know precisely how AIM2 affects tumorigenesis, so two independent teams investigated its role.

In one study, Justin Wilson, PhD, of the University of North Carolina in Chapel Hill, and colleagues dosed mice with two compounds that induce colon tumors. Mice lacking AIM2 developed more precancerous intestinal polyps and colon tumors than did controls. The researchers also studied mice that carry a mutation in the gene adenomatous polyposis coli. In humans, this gene is mutated in many sporadic colon cancers and a hereditary form of the disease. Mice with the mutation spontaneously developed colorectal and intestinal tumors, and the team determined that losing AIM2 increased their tumor load.

The researchers found that colon tissue from the AIM2-lacking mice showed increased levels of activated AKT. A promoter of cell survival and proliferation, AKT is often overactive in tumors. As Wilson and colleagues reported in *Nature Medicine*, AIM2 teams up with the protein DNA-PK to block AKT (Nat Med 2015 June 24 [Epub ahead of print]).

In the other study, Thirumala-Devi Kanneganti, PhD, of St. Jude Children's Research Hospital in Memphis, TN, and colleagues discovered that AIM2 also curbs tumor growth by curtailing proliferation of stem cells from the colon epithelium (Cell 2015;162:45–58). In culture, these cells divided more rapidly if they were missing AIM2. The team also saw increased intestinal stem cell proliferation and faster tumor growth in mice that lacked AIM2.

The protein might also influence tumor growth by controlling the composition of the intestinal microbiota. AIM2's absence altered the abundance of several bacterial species—including two species linked to colon tumors—the researchers reported.

Both studies agree that AIM2's ability to suppress tumor growth is independent of its function as an inflammasome protein. Both suggest that AIM2 inhibits AKT, and both point to avenues for therapy or prevention.

Wilson and colleagues gave the same tumor-inducing compounds they'd used before to AIM2-lacking mice. One group of animals also received an AKT blocker, and those mice developed fewer polyps and tumors than did mice that received a placebo.

"If you can inhibit AKT, you might be able to treat tumors" in which AIM2 is scarce or absent, says Jenny P.Y. Ting, PhD, senior author of the *Nature Medicine* paper. No AKT inhibitors are approved for treating cancer, but several are in development.

Kanneganti's team evaluated whether changes in the animals' intestinal microbiota reduced tumor formation. They housed AIM2-lacking mice with normal animals. The rodents slowly acquired